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reduce the oxidizing species, hydrogen peroxide, to less harmful molecules. Thus, the artisan would take from this reference the clear message that oxidation can damage cells and that molecules which disarm oxidants, i.e., antioxidants, should help protect the integrity of cells.

While neither ZIKRA nor WEISS mentions the role of cyclic adenosine monophosphate (cAMP) in protecting cells from oxidative damage, MUNKRES does teach that dietary cAMP induces superoxide dismutase in short-lived mutants of *Neurospora*. The authors hypothesize that dietary antioxidants may enhance the survival of *Neurospora* by supplanting the function of any deficient antioxygenic enzymes.

While neither ZIKRIA nor WEISS nor MUNKRES teaches the value of hydroxyethyl rutoside as an antioxidant, GERDIN does teach that hydroxyethyl rutoside acts as **an antioxidant to prevent the leakage of serum proteins from capillary junctions**.

In summary, WEISS, MUNKRES, and GERDIN teach that at the time of the invention the artisan would have known that superoxide dismutase, glutathione peroxidase, catalase, hydroxyethyl rutoside, and cAMP are each antioxidants or induces of antioxidants. Vitamin C is the world best known naturally occurring antioxidant which even the non-artisan would recognize immediately as an antioxidant. Such antioxidants are protectors of cells by eliminating strongly oxidizing and free radical molecules. Therefore, it would have been obvious to the person of ordinary skill in the art at the time of the invention to have modified ZIKRIA's method for preventing leakage of serum proteins from capillary endothelial junctions during increased capillary permeability and the compositions of hydroxyethyl starch

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used therein, by adding one or more of the art recognized, non-toxic antioxidants taught by WEISS, MUNKRES, or GERDIN or otherwise known by the public (i.e., vitamin C) for the expressed purpose of protecting all cells of the body, including the cells that form the capillary endothelial junctions from oxidative and free radical damage that would increase membrane permeability, and thus lead to leakage of serum proteins. The use of normal saline, 5 % dextrose, or Ringer's lactate as the carrier solution is described in ZIKRIA (column 2, lines 9 - 13). The necessary concentration of the hydroxyethyl dextran or starch as taught by ZIKRIA (6%) falls within the range specified by claim 19. The concentrations of each of the antioxidants are either well known in the art or can be readily determined in amounts below the toxic threshold. Consequently, the instantly claimed method for preventing leakage of serum proteins from capillary endothelial junctions and the corresponding compositions is prima facie obvious in the absence of clear and convincing evidence to the contrary.

**(11) Arguments**

First of all, it is important to recognize that all of the information about antioxidants which appellant summarizes on page 3, line 5 to page 4, line 5 was known in the prior art. While appellant does not cite a source for this information, neither does he suggest in any way that such basic knowledge about antioxidants is part of appellant's invention. Therefore, the issue of this appeal focuses solely upon the combining of one or more art-recognized antioxidants with an art-recognized solution of hydroxyethyl starch or dextran for the purpose of preventing leakage of serum proteins from capillary endothelial junctions during periods of

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high capillary permeability (i.e., trauma) and/or reducing oxidative and free radical cellular damage that will increase membrane permeability and thereby allow leakage of serum proteins.

First, the appellant argues that it is not "simple logic" to use antioxidants for the art-recognized benefit of preventing cellular damage from free radicals generated by active oxygen species. This argument has been fully considered but is not deemed persuasive. When a patient has experienced severe trauma and is about to go into shock, his body is losing the ability to maintain proper body temperature (thus the mandate to keep the patient warm) and hydration (thus the need to an i.v.). Protecting all body cells from further oxidative and free radical stress by giving non-toxic antioxidants known to protect cells from oxidative free radical damage, would certainly seem to be eminently reasonable and logical.

On page 5, last full sentence of the brief, the appellant writes "The antioxidants are given in great extent because of the threat to the integrity of cells from the uncontrolled activity of free radicals." Appellant's reason for using antioxidants is also incorporated into claim 1 as a "Method of treating human subject to prevent leakage of serum proteins from capillary endothelial junctions while simultaneously preventing the harmful effect of free radical on cellular membranes and other organelles . . . ." **This statement is a clear acknowledgment that the appellant is using known antioxidants for their known and art recognized benefits: to protect cells from oxidative and free radical (superoxide and hydroxyl radicals) damage!**

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In response to appellant's argument against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See In Keller, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); In re Merck & Co., 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

In response to applicant's argument that there is no suggestion to combine the references (brief, page 7, first full sentence) the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See In re Fine, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and In re Jones, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case the motivation to combine comes from the knowledge generally available to the artisan that it is prudent to protect the all cells of a person from free radical damage by administering antioxidants, otherwise known as free radical scavengers. Even when there is no immediate emergency, millions of people take antioxidants like vitamin C and vitamin E in order to prevent oxidative damage and free radical damage to their cells, and thus, to maintain good general health. However, for the person who has experienced trauma, when speed of treatment is critical, adding an antioxidant like vitamin C to the i.v. drip allows for more rapid distribution throughout the body for immediate benefit.

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With regard to the Gerdin reference which teaches that **hydroxyethylrutoside effectively inhibits microvascular permeability**, the appellant argues that hydroxyethylrutoside is used in the instant method as an antioxidant to combat free radical damage. This argument has been fully considered but is not deemed persuasive. Antioxidants are also known free radical scavengers. Furthermore, the instant claims are directed to a method for preventing leakage of serum proteins. The combination of hydroxyethyl starch with a second compound also known to reduce microvascular permeability would have been obvious to the artisan wanting to obtain the combined benefits of two compounds that reduce the leakage serum proteins at capillary endothelial junctions.

Lastly, the appellant argues that the fact situation of Ex parte Levengood is relevant to this appeal. In Levengood, the Board of Patent Appeals and Interferences reversed the examiner's obviousness rejection over three prior art references because of a lack of motivation which created a situation of improper hindsight reconstruction. This argument has been fully considered but is also not deemed persuasive. In Levengood the examiner only established that the prior art had the skill to carry out the requisite process steps, but without the necessary motivation to do so. In contrast, in the instant appeal, the antioxidants are taught in the prior art as compounds which will protect living cells from oxidative damage and free radical damage. Furthermore, the prior art (GERDIN) teaches that one of the antioxidants, hydroxyethylrutoside, can reduce microvascular permeability, meaning that there would be reduced leakage of serum proteins. Consequently, since one antioxidant reduces

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microvascular permeability, one would reasonably expect other antioxidants to also reduce microvascular permeability in the same manner--by protecting cells from oxidative and free radical damage. Thus, the prior art would have motivated the artisan to combine one or more known antioxidants along with hydroxyethyl starch for the purpose of obtaining the combined benefits of these compounds which should reasonably result in a further reduction in the leakage of serum proteins because the endothelial capillary cells have not been so damaged by oxidation and free radicals.

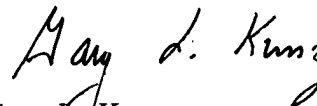
For all of the above reasons, it is believed that the obviousness rejection of claims 1 - 20 should be sustained.

Respectfully submitted,

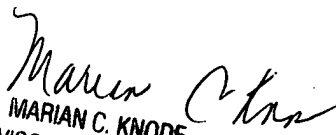


GARY GEIST  
SUPERVISORY PATENT EXAMINER  
TECH CENTER 1600

*Conferee*



Gary L. Kunz  
Art Unit 1623



MARIAN C. KNODE  
SUPERVISORY PATENT EXAMINER  
TECHNOLOGY CENTER 1700













Attachment A  
List of Assigned Issued Patents and Pending Cases

Thomson Reference Number	Country	Application number	Filing date	Patent number	Issue date	Title of the invention
[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]
[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]
[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]
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[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]
[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]
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[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]
[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]
[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]
D95005	US	08/675,636	7/1/1996			Interactive television system and method for displaying web-like stills with hyperlinks
[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]
[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]
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[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]



**Attachment A**  
**List of Assigned Issued Patents and Pending Cases**

<b>Thomson Reference Number</b>	<b>Country</b>	<b>Application number</b>	<b>Filing date</b>	<b>Patent number</b>	<b>Issue date</b>	<b>Title of the invention</b>
[REDACTED]						

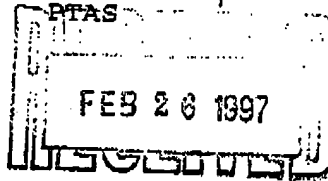


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FEBRUARY 18, 1997

CONLEY, ROSE & TAYON, P.C.  
JEFFREY C. HOOD  
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RECORDATION DATE: 10/10/1996

REEL/FRAME: 6263/0791  
NUMBER OF PAGES: 3

BRIEF: ASSIGNMENT OF ASSIGNOR'S INTEREST (SEE DOCUMENT FOR DETAILS).

ASSIGNOR:  
BROADWIN, ELLIOT

DOC DATE: 09/18/1996

ASSIGNOR:  
HAASS, JON

DOC DATE: 09/18/1996

ASSIGNEE:  
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SERIAL NUMBER: 08675636  
PATENT NUMBER:

FILING DATE: 07/01/1996  
ISSUE DATE:

8263/0791 PAGE 2

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40-381

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To the Honorable Commissioner of Patents and Tr.

100323461

Documents or copy thereof.

## 1. Name of conveying party(ies):

Elliot Broadwin and Jon Haass

Additional name(s) of conveying party(ies) attached? ☐ Yes ☒ No

12345 U.S. PTO

## 3. Nature of Conveyance:



Assignment



Merger



Security Agreement



Change of Name



Other

Execution Date: September 18, 1996

## 2. Name and address of receiving party(ies):

Name: Thomson Consumer Electronics, Inc.

Internal Address:

Street Address: 10330 North Meridian

City Indianapolis State Indiana ZIP 46290

Name: Sun Micro Systems, Inc.

Internal Address:

Street Address: 2550 Garcia Avenue

City Mountain View State California ZIP 94043

Additional name(s) & address(es) attached? ☐ Yes ☒ No

## 4. Application number(s) or patent number(s):

If this document is being filed together with a new application, the execution date of this application is:

A. Patent Application No.(s) 08/675,636

B. Patent No.(s)

Additional numbers attached? ☐ Yes ☒ NoMRD 10/10/96  
08/675636

## 5. Name and address of party to whom correspondence concerning document should be mailed:

Name: Jeffrey C. Hood

Internal Address: Conley, Rose &amp; Tayon, P.C.

Street Address: P.O. Box 3267

City Houston State TX ZIP 77253-3267

## 6. Total number of applications and patents involved: 1

7. Total fee (37 CFR 3.41): \$ 40.00



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Jeffrey C. Hood

Name of Person Signing  
Reg. No. 35,198

Signature

October 7, 1996  
Date

Total number of pages comprising cover sheet: 3

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PATENT  
5180-00400  
D95005 [TSIA]

### ASSIGNMENT

FOR GOOD AND VALUABLE CONSIDERATION, the receipt, sufficiency and adequacy of which are hereby acknowledged, the undersigned, does hereby:


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COVENANT AND AGREE that the above is and will be binding on the heirs, assigns, representatives and successors of the undersigned and extend to the successors, assigns and nominees of the Assignee:

(Signature)  Date: 9/17/96  
Name: Elliot Broadwin

Witness Hewe' UTHEZA Date: 9/17/96

Witness \_\_\_\_\_ Date: \_\_\_\_\_

(Signature)  Date: 9/18/96  
Name: Jon Haass

Witness Hewe' UTHEZA Date: 9/18/96

Witness \_\_\_\_\_ Date: \_\_\_\_\_

Jeffrey C. Hood  
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